[0026] The disclosure additionally concerns the example of such ADAM9-binding molecules, wherein such ADAM9-binding domain comprises a heavy chain variable domain (VH) and a light chain variable domain (VL) having sequences that are at least 90%, at least 95%, or at least 99% identical to sequences selected from the group consisting of:

(a) **SEQ ID NO:17** and **SEQ ID NO:55**, respectively;

(b) **SEQ ID NO:17** and **SEQ ID NO:56**, respectively;

(c) **SEQ ID NO:18** and **SEQ ID NO:56**, respectively; and

(d) **SEQ ID NO:19** and **SEQ ID NO:57**, respectively.

[0027] The disclosure additionally concerns the example of such ADAM9-binding molecules, wherein such ADAM9-binding domain comprises a heavy chain variable domain (VH) and a light chain variable domain (VL) having the sequences selected from the group consisting of:

(a) **SEQ ID NO:17** and **SEQ ID NO:55**, respectively;
(b) **SEQ ID NO:17** and **SEQ ID NO:56**, respectively;
(c) **SEQ ID NO:18** and **SEQ ID NO:56**, respectively; and
(d) **SEQ ID NO:19** and **SEQ ID NO:57**, respectively.

[0028] The disclosure additionally concerns the example of such ADAM9-binding molecules, wherein such ADAM9-binding domain has at least a 150-fold enhancement in binding affinity to cyno ADAM9 and retains high affinity binding to human ADAM9 as compared to **MAB-A**.

[0028a] In one aspect, there is provided an ADAM9-binding molecule comprising a humanized ADAM9-binding domain, wherein said humanized ADAM9-binding domain comprises a Heavy Chain Variable (VH) Domainthat comprises a CDR_H1 Domain, a CDR_H2 Domain and a CDR_H3 Domain, and a Light Chain Variable (VL) Domain that comprises a CDR_L1 Domain, a CDR_L2 Domain, and a CDR_L3 Domain, wherein:

(A) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 37, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(B) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 38, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(C) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 39, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(D) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 40, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(E) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 41, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(F) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 42, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(G) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 43, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(H) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 44, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(I) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 45, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(J) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 46, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(K) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 10, respectively; and said CDR_L1 Domain, said CDR_L2 Domain

and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(L) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 10, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 63, 13 and 14, respectively; or

(M) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 36 and 10, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 63, 13 and 14, respectively; or

(N) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 34, 36 and 10, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 64, 13 and 65, respectively.

[0029] The disclosure additionally concerns the example of such ADAM9-binding molecules, wherein such ADAM9-binding domain comprises a CDR_H1 domain, a CDR_H2 domain, and a CDR_H3 domain and a CDR_L1 domain, a CDR_L2 domain, and a CDR_L3 domain having the sequences selected from the group consisting of:

(a) **SEQ ID NOs:8**, **35** and **37** and **SEQ ID NOs:62**, **13** and **14**, respectively;

(b) **SEQ ID NOs:8**, **35** and **38** and **SEQ ID NOs:62**, **13** and **14**, respectively;

(c) **SEQ ID NOs:8**, **35** and **39** and **SEQ ID NOs:62**, **13** and **14**, respectively;

(d) **SEQ ID NOs:8**, **35** and **40** and **SEQ ID NOs:62**, **13** and **14**, respectively;

(e) **SEQ ID NOs:8**, **35** and **41** and **SEQ ID NOs:62**, **13** and **14**, respectively;

(f) **SEQ ID NOs:8**, **35** and **42** and **SEQ ID NOs:62**, **13** and **14**, respectively;

(g) **SEQ ID NOs:8**, **35** and **43** and **SEQ ID NOs:62**, **13** and **14**, respectively;

(h) **SEQ ID NOs:8**, **35** and **44** and **SEQ ID NOs:62**, **13** and **14**, respectively;

[0044] The disclosure additionally concerns the example of such ADAM9-binding molecules, wherein such effector cell is a cytotoxic T-cell or a Natural Killer (NK) cell.

[0045] The disclosure additionally concerns the example of such ADAM9-binding molecules, wherein such first molecule present on the surface of an effector cell is CD3 and such second molecule present on the surface of an effector cell is CD8

[0046] The disclosure additionally concerns the example of such ADAM9-binding molecules, wherein such ADAM9-binding molecule mediates coordinated binding of a cell expressing ADAM9 and a cytotoxic T cell.

[0047] In one aspect, there is provided a pharmaceutical composition that comprises an effective amount of any one of the above-described ADAM9-binding molecules and a pharmaceutically acceptable carrier, excipient or diluent.

[0047a] In one aspect, there is provided use of any of the above-described ADAM9-binding molecules, or the use of the above-described pharmaceutical composition in the manufacture of a medicament for the treatment of a disease or condition associated with, or characterized by, the expression of ADAM9.

[0048] The disclosure additionally concerns the use of any of the above-described ADAM9-binding molecules, or the use of the above-described pharmaceutical composition in the treatment of a disease or condition associated with, or characterized by, the expression of ADAM9.

[0049] The disclosure particularly concerns such use wherein such disease or condition associated with, or characterized by, the expression of ADAM9 is cancer, and especially wherein such cancer is selected from the group consisting: bladder cancer, breast cancer, cervical cancer, colorectal cancer (especially an adenocarcinoma, gastrointestinal carcinoid tumors, gastrointestinal stromal tumors, primary colorectal lymphoma, leiomyosarcoma, melanoma, or squamous cell carcinoma), esophageal cancer, gastric cancer, head and neck cancer, liver cancer, non-small-cell lung cancer (especially a squamous cell carcinoma, adenocarcinoma, or large-cell undifferentiated carcinoma), myeloid cancer, ovarian cancer, pancreatic cancer, prostate cancer, renal cell carcinoma, thyroid cancer, testicular cancer, and uterine cancer.

[0050] The disclosure additionally concerns a method for treating a disease or condition associated with, or characterized by, the expression of ADAM9 in a subject comprising administering to such subject an effective amount of any of the above-described ADAM9-binding molecules, or any of the above-described pharmaceutical compositions.

WHAT IS CLAIMED IS:

Claim 1. An ADAM9-binding molecule comprising a humanized ADAM9-binding domain, wherein said humanized ADAM9-binding domain comprises a Heavy Chain Variable (VH) Domain that comprises a CDR_H1 Domain, a CDR_H2 Domain and a CDR_H3 Domain, and a Light Chain Variable (VL) Domain that comprises a CDR_L1 Domain, a CDR_L2 Domain, and a CDR_L3 Domain, wherein:

(A) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 37, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(B) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 38, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(C) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 39, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(D) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 40, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(E) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 41, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(F) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 42, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(G) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 43, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(H) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 44, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(I) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 45, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(J) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 46, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(K) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 10, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively; or

(L) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 10, respectively; and said CDR_L1 Domain, said CDR_L2 Domain

and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 63, 13 and 14, respectively; or

(M) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 8, 36 and 10, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 63, 13 and 14, respectively; or

(N) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain comprise the amino acid sequences of SEQ ID NOs: 34, 36 and 10, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain comprise the amino acid sequences of SEQ ID NOs: 64, 13 and 65, respectively.

Claim 2. The ADAM9-binding molecule of claim 1, wherein said humanized ADAM9-binding domain comprises:

(A) (1) said CDR_H1 Domain that comprises the amino acid sequence of SEQ ID NO:8;

(2) said CDR_H2 Domain that comprises the amino acid sequence of SEQ ID NO:35; and

(3) said CDR_H3 Domain that comprises the amino acid sequence of: SEQ ID NO: 37, 38, 39, 40, 41, 42, 43, 44, 45 or 46;

and

(B) (1) said CDR_L1 Domain that comprises the amino acid sequence of SEQ ID NO:62;

(2) said CDR_L2 Domain that comprises the amino acid sequence of SEQ ID NO:13; and

(3) said CDR_L3 Domain that comprises the amino acid sequence of SEQ ID NO:14.

Claim 3. The ADAM9-binding molecule of claim 2, wherein said humanized ADAM9-binding domain comprises:

(A) (1) said CDR_H1 Domain that comprises the amino acid sequence SYWMH (**SEQ ID NO:8**);

(2) said CDR_H2 Domain that comprises the amino acid sequence EIIPIFGHTNYNEKFKS (**SEQ ID NO:35**); and

(3) said CDR_H3 Domain that comprises the amino acid sequence GGYYYYPRQGFLDY (**SEQ ID NO:45**);

and

(B) (1) said CDR_L1 Domain that comprises the amino acid sequence KASQSVDYSGDSYMN (**SEQ ID NO:62**);

(2) said CDR_L2 Domain that comprises the amino acid sequence AASDLES (**SEQ ID NO:13**); and

(3) said CDR_L3 Domain that comprises the amino acid sequence QQSHEDPFT (**SEQ ID NO:14**).

Claim 4. The ADAM9-binding molecule of any one of claims 1-3, wherein said humanized ADAM9-binding domain comprises:

(A) said VH Domain that comprises the amino acid sequence of **SEQ ID NO:20**, **SEQ ID NO: 21**, **SEQ ID NO:22**, **SEQ ID NO:23**, **SEQ ID NO:24**, **SEQ ID NO:25**, **SEQ ID NO:26**, **SEQ ID NO:27**, **SEQ ID NO:28** or **SEQ ID NO:29**; and

(B) said VL Domain that comprises the amino acid sequence of **SEQ ID NO:55**.

Claim 5. The ADAM9-binding molecule of any one of claims 1-3, wherein said humanized ADAM9-binding domain comprises:

(A) said VH Domain that comprises the amino acid sequence of **SEQ ID NO: 17**, and said VL Domain that comprises the amino acid sequence of **SEQ ID NO:55**; or

(B) said VH Domain that comprises the amino acid sequence of **SEQ ID NO: 17**, and said VL Domain that comprises the amino acid sequence of **SEQ ID NO:56**; or

(C) said VH Domain that comprises the amino acid sequence of **SEQ ID NO: 18**, and said VL Domain that comprises the amino acid sequence of **SEQ ID NO:56**; or

(D) said VH Domain that comprises the amino acid sequence of **SEQ ID NO: 19**, and said VL Domain that comprises the amino acid sequence of **SEQ ID NO:57**.

Claim 6. The ADAM9-binding molecule of claim 4, wherein said humanized ADAM9-binding domain comprises the VH Domain of **SEQ ID NO:28**.

Claim 7. The ADAM9-binding molecule of any one of claims 1-6, wherein said molecule is a monospecific ADAM9-binding antibody or an ADAM9-binding fragment thereof.

Claim 8. The ADAM9-binding molecule of any one of claims 1-6, wherein said molecule is a bispecific antibody.

Claim 9. The ADAM9-binding molecule of any one of claims 1-6, wherein said molecule is a diabody, said diabody being a covalently bonded complex that comprises two, three, four or five polypeptide chains.

Claim 10. The ADAM9-binding molecule of any one of claims 1-6, wherein said molecule is a trivalent binding molecule, said trivalent binding molecule being a covalently bonded complex that comprises three, four, five, or more polypeptide chains.

Claim 11. The ADAM9-binding molecule of any one of claims 7-10, wherein said ADAM9-binding molecule comprises an Fc Region selected from the group consisting of: IgG1, IgG2, IgG3 and IgG4.

Claim 12. The ADAM9-binding molecule of claim 11, wherein said Fc Region is a variant Fc Region that comprises, relative to a wild-type Fc Region, one or more amino acid modification(s) that:

(a) reduce(s) the affinity of the variant Fc Region for an FcγR, relative to that exhibited by the wild-type Fc Region; and/or

(b) enhance(s) the serum half-life of said ADAM9-binding molecule, relative to a comparable molecule comprising the wild-type Fc Region.

Claim 13. The ADAM9-binding molecule of claim 12, wherein said one or more amino acid modification(s) that reduce(s) the affinity of the variant Fc Region for an FcγR comprise:

(A) L234A;

(B) L235A; or

(C) L234A and L235A;

wherein said numbering is that of the EU index as in Kabat.

Claim 14. The ADAM9-binding molecule of any one of claims 12-13, wherein said one or more amino acid modification(s) that that enhance(s) the serum half-life of said ADAM9-binding molecule comprise:

(A) M252Y;

(B) M252Y and S254T;

(C) M252Y and T256E;

(D) M252Y, S254T and T256E; or

(E) K288D and H435K;

wherein said numbering is that of the EU index as in Kabat.

Claim 15. The ADAM9-binding molecule of any one of claims 1-14, wherein said molecule further comprises a human IgG Constant CL Kappa Domain having the amino acid sequence of SEQ ID NO:101.

Claim 16. The ADAM9-binding molecule of claim 15, wherein said molecule comprises:

(a) said CDR_H1 Domain, said CDR_H2 Domain and said CDR_H3 Domain that comprise the amino acid sequences of SEQ ID NOs: 8, 35 and 45, respectively; and said CDR_L1 Domain, said CDR_L2 Domain and said CDR_L3 Domain that comprise the amino acid sequences of SEQ ID NOs: 62, 13 and 14, respectively;

(b) an Fc Region of IgG1, wherein said Fc Region is a variant Fc Region that comprises amino acid modifications M252Y, S254T and T256E, wherein said numbering is that of the EU index as in Kabat.

Claim 17. The ADAM9-binding molecule of any one of claims 1-9 or 11-16, wherein said molecule is bispecific and comprises an epitope-binding site capable of

immunospecific binding to an epitope of ADAM9 and an epitope-binding site capable of immunospecific binding to an epitope of a molecule present on the surface of an effector cell.

Claim 18. The ADAM9-binding molecule of claim 17, wherein said molecule comprises two epitope-binding sites capable of immunospecific binding to epitope(s) of ADAM9 and two epitope-binding sites capable of immunospecific binding to epitope(s) of a molecule present on the surface of an effector cell.

Claim 19. The ADAM9-binding molecule of any one of claims 1-6 or 10-16, wherein said molecule is trispecific and comprises:

(a) one epitope-binding site capable of immunospecific binding to an epitope of ADAM9;

(b) one epitope-binding site capable of immunospecific binding to an epitope of a first molecule present on the surface of an effector cell; and

(c) one epitope-binding site capable of immunospecific binding to an epitope of a second molecule present on the surface of an effector cell.

Claim 20. The ADAM9-binding molecule of any one of claims 17-19, wherein said molecule present on the surface of an effector cell is CD2, CD3, CD8, TCR, or NKG2D.

Claim 21. A pharmaceutical composition that comprises an effective amount of the ADAM9-binding molecule of any one of claims 1-20 and a pharmaceutically acceptable carrier, excipient or diluent.

Claim 22. Use of the ADAM9-binding molecule of any one of claims 1-20, or the pharmaceutical composition of claim 21, in the manufacture of a medicament for the treatment of a disease or condition associated with, or characterized by, the expression of ADAM9.

Claim 23. The use of claim 22, wherein said disease or condition associated with, or characterized by, the expression of ADAM9 is a cancer selected from the group consisting of: bladder cancer, breast cancer, cervical cancer, colorectal cancer, esophageal cancer, gastric cancer, head and neck cancer, liver cancer, non-small-cell lung cancer, myeloid cancer, ovarian cancer, pancreatic cancer, prostate cancer, renal cell carcinoma, thyroid cancer, testicular cancer, and uterine cancer.